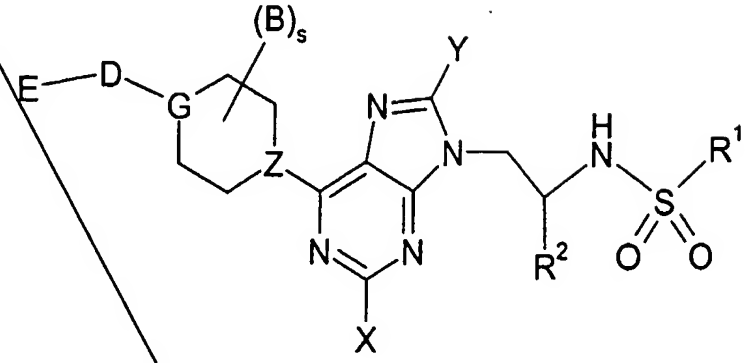
Patent claims

Amex. A2

1. A compound of the formula I



I

wherein

B is (C_1-C_{18})-alkyl, (C_3-C_{14})-cycloalkyl, (C_3-C_{14})-cycloalkyl-(C_1-C_8)-alkyl-, (C_5-C_{14})-aryl, (C_5-C_{14})-aryl-(C_1-C_8)-alkyl-, (C_5-C_{14})-heteroaryl, (C_5-C_{14})-heteroaryl-(C_1-C_8)-alkyl-, fluorine, chlorine, bromine, hydroxy, cyano, trifluoromethyl, nitro, hydroxycarbonyl-, (C_1-C_6)-alkoxy, (C_1-C_6)-alkoxy-(C_1-C_6)-alkyl-, (C_1-C_6)-alkoxycarbonyl-, (C_1-C_6)-alkylcarbonyl-, (C_5-C_{14})-arylcarbonyl-, (C_1-C_6)-alkylaminocarbonyl-, (C_1-C_6)-alkoxy-(C_1-C_6)-alkoxy-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylcarbonyl-, (C_1-C_6)-alkanoylamino-, (C_1-C_6)-alkylsulfonylamino-, (C_5-C_{14})-arylsulfonylamino-, (C_1-C_6)-alkylamino-, di-$((C_1-C_6)$-alkyl)amino-, (C_1-C_6)-alkylsulfonyl-, aminosulfonyl-, (C_5-C_{14})-arylsulfonyl-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylsulfonyl-, (C_5-C_{14})-aryl or (C_5-C_{14})-heteroaryl, where all residues B are independent of one another and can be identical or different, or B denotes an aromatic or non-aromatic ring system that is fused to the 6-membered ring containing the groups G and Z;

D is $-C(O)-N(R^6)-$, $-NR^6-C(O)-$, $-NR^6-C(O)-N(R^6)-$, $-NR^6-C(S)-N(R^6)-$, $-C(S)-N(R^6)-$ or $-C(R^6)=N-N(R^6)-$, where the divalent residues representing D are bonded to the group E via the free bond on their right side;

E is a residue from the series consisting of

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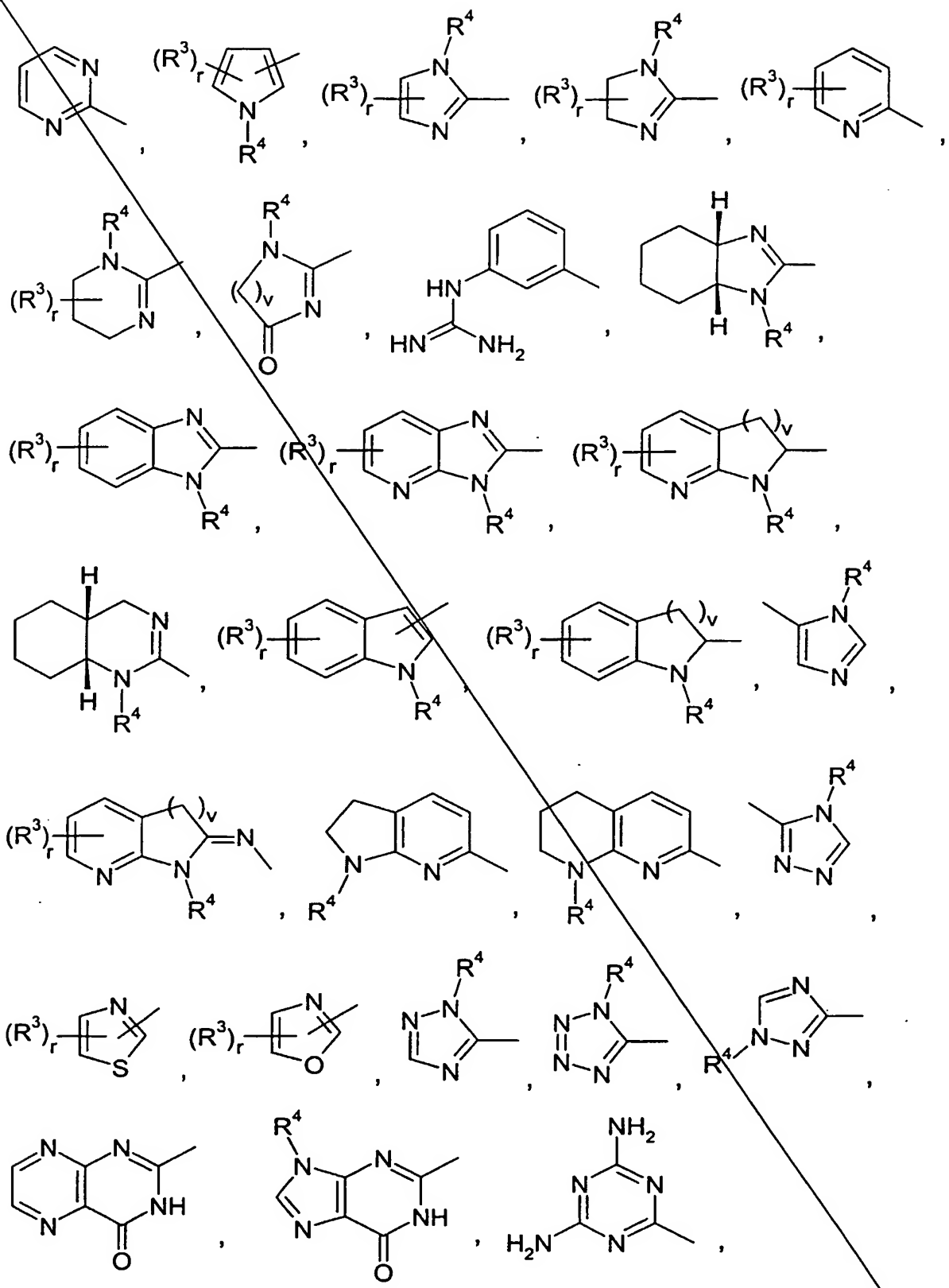

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contd. A2

R^6-C(=NR^6)-NR^6- and $R^6R^{6'}$N-C(=NR^6)-;

G is N, CH or C($(C_1$-$C_4)$-alkyl);

X is hydrogen, -$NR^6R^{6'}$, fluorine, chlorine, bromine, -OR^6, -SR^6, hydroxy-$(C_1$-$C_6)$-alkyl-NH-, (hydroxy-$(C_1$-$C_6)$-alkyl)$_2$N-, amino-$(C_1$-$C_6)$-alkyl-NH-, (amino-$(C_1$-$C_6)$-alkyl)$_2$N-, hydroxy-$(C_1$-$C_6)$-alkyl-O-, hydroxy-$(C_1$-$C_6)$-alkyl-S- or -NH-C(O)-R^6;

Y has one of the meanings of R^6 or is fluorine, chlorine, bromine, cyano, -$NR^6R^{6'}$, -OR^6, -SR^6 or hydroxy-$(C_1$-$C_6)$-alkyl-NH-;

Z is N or CH;

R^1 is $(C_1$-$C_{18})$-alkyl, $(C_3$-$C_{14})$-cycloalkyl, $(C_3$-$C_{14})$-cycloalkyl-$(C_1$-$C_8)$-alkyl-, $(C_5$-$C_{14})$-aryl, $(C_5$-$C_{14})$-aryl-$(C_1$-$C_8)$-alkyl-, $(C_5$-$C_{14})$-heteroaryl or $(C_5$-$C_{14})$-heteroaryl-$(C_1$-$C_8)$-alkyl- where aryl, heteroaryl, cycloalkyl and alkyl can be substituted one, two or three times by identical or different substituents from the series consisting of fluorine, chlorine, bromine, cyano, trifluoromethyl, nitro, hydroxycarbonyl-, $(C_1$-$C_6)$-alkyl, $(C_1$-$C_6)$-alkoxy, $(C_1$-$C_6)$-alkoxy-$(C_1$-$C_6)$-alkyl-, $(C_1$-$C_6)$-alkoxycarbonyl-, $(C_1$-$C_6)$-alkylcarbonyl-, $(C_1$-$C_6)$-alkylaminocarbonyl-, $(C_1$-$C_8)$-alkoxy-$(C_1$-$C_6)$-alkoxy-, $(C_5$-$C_{14})$-arylcarbonyl-, $(C_5$-$C_{14})$-aryl-$(C_1$-$C_8)$-alkylcarbonyl-, $(C_1$-$C_6)$-alkanoylamino-, $(C_5$-$C_{14})$-arylsulfonylamino-, $(C_1$-$C_6)$-alkylsulfonylamino-, $(C_1$-$C_6)$-alkylamino-, di-$((C_1$-$C_6)$-alkyl)amino-, $(C_1$-$C_6)$-alkylsulfonyl-, $(C_1$-$C_6)$-alkylaminosulfonyl-, $(C_5$-$C_{14})$-arylaminosulfonyl-, $(C_5$-$C_{14})$-aryl-$(C_1$-$C_8)$-alkylaminosulfonyl-, $(C_5$-$C_{14})$-arylsulfonyl-, $(C_5$-$C_{14})$-aryl-$(C_1$-$C_8)$-alkylsulfonyl-, $(C_5$-$C_{14})$-aryl and $(C_5$-$C_{14})$-heteroaryl;

R^2 is -C(O)R^5, -C(S)R^5, -$S(O)_pR^5$, -P(O)$R^5R^{5'}$ or a residue of a 4-membered to 8-membered saturated or unsaturated heterocycle which contains 1, 2, 3 or 4 heteroatoms from the series consisting of nitrogen, oxygen and sulfur;

R^3 is $(C_1$-$C_{18})$-alkyl, $(C_3$-$C_{14})$-cycloalkyl, $(C_3$-$C_{14})$-cycloalkyl-$(C_1$-$C_8)$-alkyl-, $(C_5$-$C_{14})$-aryl, $(C_5$-$C_{14})$-aryl-$(C_1$-$C_8)$-alkyl-, $(C_5$-$C_{14})$-heteroaryl, $(C_5$-$C_{14})$-heteroaryl-$(C_1$-$C_8)$-

contd. A2

alkyl-, fluorine, chlorine, bromine, hydroxy, cyano, trifluoromethyl, nitro, hydroxycarbonyl-, (C_1-C_6)-alkoxy, (C_1-C_6)-alkoxy-(C_1-C_6)-alkyl-, (C_1-C_6)-alkoxycarbonyl-, (C_1-C_6)-alkylcarbonyl-, (C_5-C_{14})-arylcarbonyl-, (C_1-C_6)-alkylaminocarbonyl-, (C_1-C_6)-alkoxy-(C_1-C_6)-alkoxy-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylcarbonyl-, (C_1-C_6)-alkanoylamino-, (C_1-C_6)-alkylsulfonylamino-, (C_5-C_{14})-arylsulfonylamino-, (C_1-C_6)-alkylamino-, di-((C_1-C_6)-alkyl)amino-, (C_1-C_6)-alkylsulfonyl-, aminosulfonyl-, (C_5-C_{14})-arylsulfonyl-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylsulfonyl-, (C_5-C_{14})-aryl or (C_5-C_{14})-heteroaryl, where all residues R^3 are independent of one another and can be identical or different;

R^4 is hydrogen, (C_1-C_{10})-alkyl, (C_3-C_{14})-cycloalkyl, (C_3-C_{14})-cycloalkyl-(C_1-C_8)-alkyl-, (C_5-C_{14})-aryl or (C_5-C_{14})-aryl-(C_1-C_8)-alkyl-;

R^5 and $R^{5'}$ are hydroxy, (C_1-C_8)-alkoxy, (C_5-C_{14})-aryl-(C_1-C_8)-alkoxy-, (C_1-C_8)-alkylcarbonyloxy-(C_1-C_4)-alkoxy-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylcarbonyloxy-(C_1-C_8)-alkoxy- or $-NR^6R^{6'}$, where the residues R^5 and $R^{5'}$ are independent of one another and can be identical or different;

R^6 and $R^{6'}$ are hydrogen, (C_1-C_{18})-alkyl, (C_3-C_{14})-cycloalkyl, (C_3-C_{14})-cycloalkyl-(C_1-C_8)-alkyl-, (C_5-C_{14})-aryl where in the aryl residue one, two, three, four or five ring carbon atoms can be replaced by heteroatoms from the series consisting of nitrogen, oxygen and sulfur, or (C_5-C_{14})-aryl-(C_1-C_8)-alkyl- where in the aryl moiety of the aryl-alkyl- residue one, two, three, four or five ring carbon atoms can be replaced by heteroatoms from the series consisting of nitrogen, oxygen and sulfur,
or R^6 and $R^{6'}$ together with the nitrogen atom to which they are bonded form a 4-membered to 8-membered ring system which in addition to the nitrogen atom to which R^6 and $R^{6'}$ are bonded can contain one, two or three ring heteroatoms from the series consisting of nitrogen, oxygen and sulfur and which can be unsaturated or saturated,
where all residues R^6 and $R^{6'}$ are independent of one another and can be identical or

contd. A2

r is zero, one, two, three or four;

s is zero, one, two, three or four;

v is one, two or three;

p is one or two;

in all their stereoisomeric forms and mixtures thereof in all ratios, and their physiologically tolerable salts and their prodrugs;

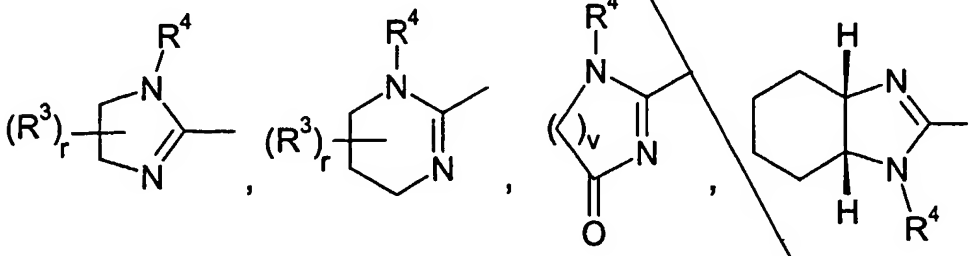
where, instead of the purine structure shown in formula I, also a 3-deazapurine structure, a 7-deazapurine structure or a 7-deaza-8-azapurine structure can be present.

2. A compound of the formula I as claimed in claim 1, wherein

B is (C_1-C_{18})-alkyl or hydroxy, where all residues B are independent of one another and can be identical or different;

D is -C(O)-N(R^6)-, where this divalent residue is bonded to the group E via its nitrogen atom;

E is a residue from the series consisting of



and $R^6R^{6'}N$-C(=NR^6)-;

G is N or CH;

X is hydrogen;

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Y is hydrogen;

Z is N or CH;

R^1 is (C_1-C_{18})-alkyl, (C_3-C_{14})-cycloalkyl, (C_3-C_{14})-cycloalkyl-(C_1-C_8)-alkyl-, (C_5-C_{14})-aryl, (C_5-C_{14})-aryl-(C_1-C_8)-alkyl-, (C_5-C_{14})-heteroaryl or (C_5-C_{14})-heteroaryl-(C_1-C_8)-alkyl- where aryl, heteroaryl, cycloalkyl and alkyl can be substituted one, two or three times by identical or different substituents from the series consisting of fluorine, chlorine, bromine, cyano, trifluoromethyl, nitro, hydroxycarbonyl-, (C_1-C_6)-alkyl, (C_1-C_6)-alkoxy, (C_1-C_6)-alkoxy-(C_1-C_6)-alkyl-, (C_1-C_6)-alkoxycarbonyl-, (C_1-C_6)-alkylcarbonyl-, (C_1-C_6)-alkylaminocarbonyl-, (C_1-C_6)-alkoxy-(C_1-C_6)-alkoxy-, (C_5-C_{14})-arylcarbonyl-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylcarbonyl-, (C_1-C_6)-alkanoylamino-, (C_5-C_{14})-arylsulfonylamino-, (C_1-C_6)-alkylsulfonylamino-, (C_1-C_6)-alkylamino-, di-$((C_1-C_6)$-alkyl)amino-, (C_1-C_6)-alkylsulfonyl-, (C_1-C_6)-alkylaminosulfonyl-, (C_5-C_{14})-arylaminosulfonyl-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylaminosulfonyl-, (C_5-C_{14})-arylsulfonyl-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylsulfonyl-, (C_5-C_{14})-aryl and (C_5-C_{14})-heteroaryl;

R^2 is $-C(O)R^5$;

R^3 is (C_1-C_6)-alkyl, (C_3-C_{14})-cycloalkyl, (C_3-C_{14})-cycloalkyl-(C_1-C_8)-alkyl-, fluorine, chlorine, bromine, cyano, trifluoromethyl, hydroxy or (C_1-C_6)-alkoxy, where all residues R^3 are independent of one another and can be identical or different;

R^4 is hydrogen or (C_1-C_6)-alkyl;

R^5 is hydroxy or (C_1-C_8)-alkoxy;

R^6 and $R^{6'}$ are hydrogen, (C_1-C_6)-alkyl, (C_3-C_{14})-cycloalkyl, (C_3-C_{14})-cycloalkyl-(C_1-C_8)-alkyl-, (C_5-C_{14})-aryl where in the aryl residue one, two or three ring carbon atoms can be replaced by heteroatoms from the series consisting of nitrogen, oxygen and sulfur, or (C_5-C_{14})-aryl-(C_1-C_8)-alkyl-, where in the aryl moiety of the aryl-alkyl- residue

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one, two or three ring carbon atoms can be replaced by heteroatoms from the series consisting of nitrogen, oxygen and sulfur,

or R^6 and $R^{6'}$ together with the nitrogen atom to which they are bonded form a 4-membered to 6-membered ring system which in addition to the nitrogen atom to which R^6 and $R^{6'}$ are bonded can contain one, two or three ring heteroatoms from the series consisting of nitrogen, oxygen and sulfur and which can be unsaturated or saturated,

where all residues R^6 and $R^{6'}$ are independent of one another and can be identical or different;

r is zero, one, two, three or four;

s is zero, one, two, three or four;

v is one, two or three;

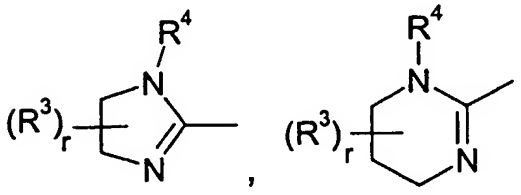
in all their stereoisomeric forms and mixtures thereof in all ratios, and their physiologically tolerable salts and their prodrugs.

3. A compound of the formula I as claimed in claims 1 and/or 2, wherein

B is (C_1-C_6)-alkyl or hydroxy, where all residues B are independent of one another and can be identical or different;

D is -C(O)-N(R^6)-, where this divalent residue is bonded to the group E via its nitrogen atom;

E is a residue from the series consisting of



and $R^6R^{6'}N$-C(=NR^6)-;

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G is N or CH;

X is hydrogen;

Y is hydrogen;

Z is N;

R^1 is (C_1-C_{18})-alkyl, (C_3-C_{14})-cycloalkyl, (C_3-C_{14})-cycloalkyl-(C_1-C_8)-alkyl-, (C_5-C_{14})-aryl, (C_5-C_{14})-aryl-(C_1-C_8)-alkyl-, (C_5-C_{14})-heteroaryl or (C_5-C_{14})-heteroaryl-(C_1-C_8)-alkyl- where aryl, heteroaryl, cycloalkyl and alkyl can be substituted one, two or three times by identical of different substituents from the series consisting of fluorine, chlorine, bromine, cyano, trifluoromethyl, nitro, hydroxycarbonyl-, (C_1-C_6)-alkyl, (C_1-C_6)-alkoxy, (C_1-C_6)-alkoxy-(C_1-C_6)-alkyl-, (C_1-C_6)-alkoxycarbonyl-, (C_1-C_6)-alkylcarbonyl-, (C_1-C_6)-alkylaminocarbonyl-, (C_1-C_6)-alkoxy-(C_1-C_6)-alkoxy-, (C_5-C_{14})-arylcarbonyl-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylcarbonyl-, (C_1-C_6)-alkanoylamino-, (C_5-C_{14})-arylsulfonylamino-, (C_1-C_6)-alkylsulfonylamino-, (C_1-C_6)-alkylamino-, di-((C_1-C_6)-alkyl)amino-, (C_1-C_6)-alkylsulfonyl-, (C_1-C_6)-alkylaminosulfonyl-, (C_5-C_{14})-arylaminosulfonyl-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylaminosulfonyl-, (C_5-C_{14})-arylsulfonyl-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylsulfonyl-, (C_5-C_{14})-aryl and (C_5-C_{14})-heteroaryl;

R^2 is -C(O)R^5;

R^3 is (C_1-C_6)-alkyl, fluorine, chlorine, bromine, cyano , hydroxy or (C_1-C_6)-alkoxy, where all residues R^3 are independent of one another and can be identical or different;

R^4 is hydrogen or (C_1-C_4)-alkyl;

R^5 is hydroxy or (C_1-C_6)-alkoxy;

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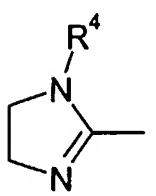
R^6 and $R^{6'}$ are hydrogen, (C_1-C_6)-alkyl, (C_3-C_{14})-cycloalkyl, (C_3-C_{14})-cycloalkyl-(C_1-C_8)-alkyl- or (C_5-C_{14})-aryl-(C_1-C_8)-alkyl-, or R^6 and $R^{6'}$ together with the nitrogen atom to which they are bonded form a 4-membered to 6-membered ring system which in addition to the nitrogen atom to which R^6 and $R^{6'}$ are bonded can contain one or two ring heteroatoms from the series consisting of nitrogen, oxygen and sulfur and which can be unsaturated or saturated,
where all residues R^6 and $R^{6'}$ are independent of one another and can be identical or different;

r is zero, one, two, three or four;
s is zero, one or two;

in all their stereoisomeric forms and mixtures thereof in all ratios, and their physiologically tolerable salts and their prodrugs.

4. A compound of the formula I as claimed in one or more of claims 1 to 3, wherein D is -C(O)-N(R^6)-, where this divalent residue is bonded to the group E via its nitrogen atom;

E is a residue from the series consisting of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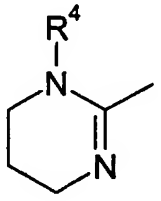

;

G is CH;

X is hydrogen;

Y is hydrogen;

contd. A2

Z is N;

R^1 is (C_1-C_{18})-alkyl, (C_3-C_{14})-cycloalkyl, (C_3-C_{14})-cycloalkyl-(C_1-C_8)-alkyl-, (C_5-C_{14})-aryl, (C_5-C_{14})-aryl-(C_1-C_8)-alkyl-, (C_5-C_{14})-heteroaryl or (C_5-C_{14})-heteroaryl-(C_1-C_8)-alkyl- where aryl, heteroaryl, cycloalkyl and alkyl can be substituted one, two or three times by identical of different substituents from the series consisting of fluorine, chlorine, bromine, cyano, trifluoromethyl, nitro, hydroxycarbonyl-, (C_1-C_6)-alkyl, (C_1-C_6)-alkoxy, (C_1-C_6)-alkoxy-(C_1-C_6)-alkyl-, (C_1-C_6)-alkoxycarbonyl-, (C_1-C_6)-alkylcarbonyl-, (C_1-C_6)-alkylaminocarbonyl-, (C_1-C_6)-alkoxy-(C_1-C_6)-alkoxy-, (C_5-C_{14})-arylcarbonyl-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylcarbonyl-, (C_1-C_6)-alkanoylamino-, (C_5-C_{14})-arylsulfonylamino-, (C_1-C_6)-alkylsulfonylamino-, (C_1-C_6)-alkylamino-, di-$((C_1-C_6)$-alkyl)amino-, (C_1-C_6)-alkylsulfonyl-, (C_1-C_6)-alkylaminosulfonyl-, (C_5-C_{14})-arylaminosulfonyl-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylaminosulfonyl-, (C_5-C_{14})-arylsulfonyl-, (C_5-C_{14})-aryl-(C_1-C_8)-alkylsulfonyl-, (C_5-C_{14})-aryl and (C_5-C_{14})-heteroaryl;

R^2 is $-C(O)R^5$;

R^4 is hydrogen or (C_1-C_4)-alkyl;

R^5 is hydroxy or (C_1-C_6)-alkoxy;

R^6 is hydrogen or (C_1-C_4)-alkyl;

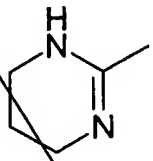
s is zero;

in all their stereoisomeric forms and mixtures thereof in all ratios, and their physiologically tolerable salts and their prodrugs.

5. A compound of the formula I as claimed in one or more of claims 1 to 4, wherein

contd. A 2

E is the residue



;

G is CH;

X is hydrogen;

Y is hydrogen;

Z is N;

R^1 is (C_1-C_{18})-alkyl, (C_3-C_{14})-cycloalkyl, (C_3-C_{14})-cycloalkyl-(C_1-C_8)-alkyl-, (C_5-C_{14})-aryl, (C_5-C_{14})-aryl-(C_1-C_8)-alkyl-, (C_5-C_{14})-heteroaryl or (C_5-C_{14})-heteroaryl-(C_1-C_8)-alkyl- where aryl, heteroaryl, cycloalkyl and alkyl can be substituted one, two or three times by identical or different substituents from the series consisting of fluorine, chlorine, bromine, cyano, trifluoromethyl, (C_1-C_6)-alkyl, (C_1-C_6)-alkoxy and (C_5-C_{14})-aryl;

R^2 is $-C(O)R^5$;

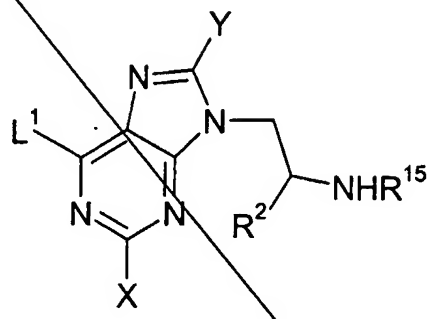
R^5 is hydroxy or (C_1-C_6)-alkoxy;

s is zero;

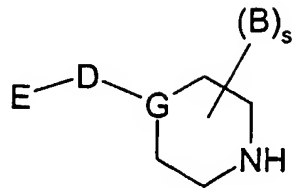
in all their stereoisomeric forms and mixtures thereof in all ratios, and their physiologically tolerable salts and their prodrugs.

6. A process for the preparation of a compound as claimed in one or more of claims 1 to 5, comprising reacting a compound of the formula V with a compound of the

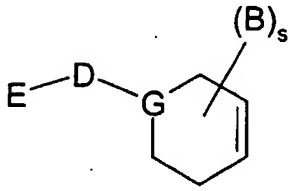
contd. A2 formula VIa or with a compound of the formula VIb



V



VIa



VIb

wherein L^1 is a leaving group, R^{15} is R^1-SO_2- or an amino protecting group and B, D, E, G, X, R^2 and s are defined as in claims 1 to 5 but where functional groups can also be present in the form of precursor groups or in protected form.

7. A pharmaceutical composition, comprising at least one compound of the formula I as claimed in one or more of claims 1 to 5 and/or its physiologically tolerable salts and/or its prodrugs and a pharmaceutically acceptable carrier.

8. A compound of the formula I as claimed in one or more of claims 1 to 5 and/or its physiologically tolerable salts and/or its prodrugs for use as a pharmaceutical.

9. A compound of the formula I as claimed in one or more of claims 1 to 5 and/or its physiologically tolerable salts and/or its prodrugs for use as a vitronectin receptor antagonist.

10. A compound of the formula I as claimed in one or more of claims 1 to 5 and/or its physiologically tolerable salts and/or its prodrugs for use as an inhibitor of bone resorption, for the therapy or prophylaxis of osteoporosis, as an inhibitor of tumor growth or tumor metastasis, as an antiinflammatory, or for the therapy or prophylaxis of cardiovascular disorders, restenoses, arteriosclerosis, nephropathies

a

~~retinopathies, psoriasis or rheumatoid arthritis.~~

add a3